REMARKS

1. Applicants hereby submit the following:

[XX] a paper copy of a "Sequence Listing", complying with §1.821(c), to be incorporated into the specification as directed above;

[ ] an amendment to the paper copy of the "Sequence Listing" submitted on , the amendment being in the form of substitute sheets;

[XX] the Sequence Listing in computer readable form, complying with §1.821(e) and §1.824, including, if an amendment to the paper copy is submitted, all previously submitted data with the amendment incorporated therein;

[ ] a substitute computer readable form to replace one found to be damaged or unreadable.

[ ] The computer readable form in this application no. 09/... is identical with that filed on .... [date sequence was filed] in application no. 09/ , filed [filing date]. In accordance with 37 C.F.R. §1.821(e), please use the [first-filed, last-filed or only, whichever is applicable] computer readable form filed in that application as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary

change in application number and filing date for the instant application. A paper copy of the Sequence Listing is [included in the originally-filed specification of the instant application, included in a separately filed preliminary amendment for incorporation into the specification, whichever is applicable].

[XX] 2. The description has been amended to comply with §1.821(d).

3. The undersigned attorney or agent hereby states as follows:

(a) this submission is not believed to include new matter [§1.821(g)];

(b) the contents of the paper copy (as amended, if applicable) and the computer readable form of the Sequence Listing, are believed to be the same [§1.821(f) and §1.825(b)];

(c) if the paper copy has been amended, the amendment is believed to be supported by the specification and is not believed to include new matter [§1.825(a)]; and

(d) if the computer readable form submitted herewith is a substitute for a form found upon receipt by the PTO to be damaged or unreadable, that the substitute data is believed to be identical to that originally filed [§1.825(d)].

4. Applicants were unable to find a scientific name for the organism for red sea turtle egg white (SEQ ID NO:103). In the SWISS-PROT Protein Sequence database, the red sea turtle egg white is entry P00993, and it is assumed that the "red sea turtle" was of the Caretta species (see enclosed Exhibit A). Applicants therefore used Caretta species as the organism for SEQ ID NO:103.

5. Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally

occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at line 6 of page 25 has been amended as follows:

We assume that ITI-D1 and EpiNE-7 have the same 3D configuration in solution as BPTI. Although EpiNE-7 and ITI-D1 are identical at positions 13, 17, 20, 32, and 39, they differ greatly in their affinities for hNE. To improve the affinity of ITI-D1 for hNE, the EpiNE-7 sequence **Val**$_{15}$-**Ala**$_{16}$-Met$_{17}$-**Phe**$_{18}$-**Pro**$_{19}$-Arg$_{20}$ (of SEQ ID NO:9) (**bold**, underscored amino acids are alterations) was incorporated into the ITI-D1 sequence by cassette mutagenesis between the *Eag*I and *Sty*I/*Nco*I sites shown in Table 35. Phage isolates containing the ITI-D1::III fusion gene with the EpiNE-7 changes around the P1 position are called MA-ITI-D1E7.

The Legend to Table 13 on pages 65-66 has been amended as follows:

1 BPTI (SEQ ID NO:87)

2 Engineered BPTI From MARK87 (SEQ ID NO:88)

3 Engineered BPTI From MARK87 (SEQ ID NO:89)

4 Bovine Colostrum (DUFT85) (SEQ ID NO:90)

5 Bovine Serum (DUFT85) (SEQ ID NO:91)

6 Semisynthetic BPTI, TSCH87 (SEQ ID NO:92)

7 Semisynthetic BPTI, TSCH87 (SEQ ID NO:93)

8 Semisynthetic BPTI, TSCH87 (SEQ ID NO:94)

9 Semisynthetic BPTI, TSCH87 (SEQ ID NO:95)

10 Semisynthetic BPTI, TSCH87 (SEQ ID NO:96)

11 Engineered BPTI, AUER87 (SEQ ID NO:97)

12 Dendroaspis polylepis polylepis (Black mamba) venom I (DUFT85) (SEQ ID NO:98)

13 Dendroaspis polylepis polylepis (Black Mamba) venom K DUFT85) (SEQ ID NO:99)

14 Hemachatus hemachates (Ringhals Cobra) HHV II (DUFT85) (SEQ ID NO:100)

15 Naja nivea (Cape cobra) NNV II (DUFT85) (SEQ ID NO:101)

16 Vipera russelli (Russel's viper) RVV II (TAKA74) (SEQ ID NO:102)

17 Red sea turtle egg white (DUFT85) (SEQ ID NO:103)

18 Snail mucus (Helix pomania) (WAGN78) (SEQ ID NO:104)

19 Dendroaspis angusticeps (Eastern green mamba) C13 S1 C3 toxin (DUFT85) (SEQ ID NO:105)

20 Dendroaspis angusticeps (Eastern Green Mamba) C13 S2 C3 toxin (DUFT85) (SEQ ID NO:106)

21 Dendroaspis polylepis polylepes (Black mamba) B toxin (DUFT85) (SEQ ID NO:107)

22 Dendroaspis polylepis polylepes (Black Mamba) E toxin

(DUFT85) (SEQ ID NO:108)

23 Vipera ammodytes TI toxin (DUFT85) (SEQ ID NO:109)

24 Vipera ammodytes CTI toxin (DUFT85) (SEQ ID NO:110)

25 Bungarus fasciatus VIII B toxin (DUFT85) (SEQ ID NO:111)

26 Anemonia sulcata (sea anemone) 5 II (DUFT85) (SEQ ID NO:112)

27 Homo sapiens HI-8e "inactive" domain (DUFT85) (SEQ ID NO:113)

28 Homo sapiens HI-8t "active" domain (DUFT85) (SEQ ID NO:114)

29 beta bungarotoxin B1 (DUFT85) (SEQ ID NO:115)

30 beta bungarotoxin B2 (DUFT85) (SEQ ID NO:116)

31 Bovine spleen TI II (FIOR85) (SEQ ID NO:117)

32 Tachypleus tridentatus (Horseshoe crab) hemocyte inhibitor (NAKA87) (SEQ ID NO:118)

33 Bombyx mori (silkworm) SCI-III (SASA84) (SEQ ID NO:119)

34 Bos taurus (inactive) BI-14 (SEQ ID NO:120)

35 Bos taurus (active) BI-8 (SEQ ID NO:121)

36:Engineered BPTI (KR15, ME52): Auerswald '88, Biol Chem Hoppe-Seyler, 369 Supplement, pp27-35 (SEQ ID NO:122).

37:Isoaprotinin G-1: Siekmann, Wenzel, Schroder, and Tschesche '88, Biol Chem Hoppe-Seyler, 369:157-163 (SEQ ID

NO:123).

38:Isoaprotinin 2: Siekmann, Wenzel, Schroder, and Tschesche '88, Biol Chem Hoppe-Seyler, 369:157-163 (SEQ ID NO:124).

39:Isoaprotinin G-2: Siekmann, Wenzel, Schroder, and Tschesche '88, Biol Chem Hoppe-Seyler, 369:157-163 (SEQ ID NO:125).

40:Isoaprotinin 1: Siekmann, Wenzel, Schroder, and Tschesche '88, Biol Chem Hoppe-Seyler, 369:157-163 (SEQ ID NO:126).

The heading at line 13-14 of page 72 has been amended as follows:

Res. Id.	EpiNE1 ~~EpiNE1~~ (SEQ ID NO:7)	Substitutions	Class

The paragraph beginning at line 8 of page 73 has been amended as follows:

Res. Id.	EpiNE1	Substitutions	Class
36	G	G strongly prefr'd; S, A prefr'd;	C
37	G	must be G so long as 38 is C	X
38	C	C strongly prefr'd	X
39	M	any	C
40	G	A,S,N,D,T,P	C
41	N	K,Q,S,D,R,T,A,E	C
42	G	any	C
43	N	must be N	X
44	N	S,K,R,T,Q,D,E	B
45	F	Y	B
46	K	any non-proline	B
47	S	T, N, A, G	B
48	A	any	B
49	E	any	A
50	D	any	A
51	C	must be C	X
52	M	any	A
53	R	any	A
54	T	any	A
55	C	must be C	X
56	G	any	A
57	G	any	A
58	A	any	A

Line 10 of page 81 has been amended as follows:

PflMI CCANNNNntgg 1 196 (SEQ ID NO:127)

Line 23 of page 81 has been amended as follows:

XcmI CCANNNNNnnnntgg 1 711 (SEQ ID NO:128)

Tables 207-208 (merged) on page 82 have been amended as follows:

TABLES 207-208 (merged)
SEQUENCES OF THE EpiNE CLONES IN THE P1 REGION

CLONE IDENTIFIERS	SEQUENCE
	13 14 15 16 17 18 19 20 21
BPTI (comp. only)	P C K A R I I R Y (BPTI) (13-21 of SEQ ID NO:6) P C V A M F Q R Y EpiNEα (13-21 of SEQ ID NO:129)
3, 9, 16, 17, 18, 19	P C V G F F S R Y EpiNE3 (13-21 of SEQ ID NO:10)
6	P C V G F F Q R Y EpiNE6 (13-21 of SEQ ID NO:11)
7, 13, 14, 15, 20	P C V A M F P R Y EpiNE7 (13-21 of SEQ ID NO:9)
4	P C V A I F P R Y EpiNE4 (13-21 of SEQ ID NO:12)
8	P C V A I F K R S EpiNE8 (13-21 of SEQ ID NO:13)
1, 10, 11, 12	P C I A F F P R Y EpiNE1 (13-21 of SEQ ID NO:7)
5	P C I A F F Q R Y EpiNE5 (13-21 of SEQ ID NO:14)
2	P C I A L F K R Y EpiNE2 (13-21 of SEQ ID NO:15)

NiceProt View of SWISS-PROT: P00993

Printer-friendly view | Quick BlastP search

[General] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

General information about the entry

Entry name	**IBP_CARCR**
Primary accession number	**P00993**
Secondary accession numbers	None
Entered in SWISS-PROT in	Release 01, July 1986
Sequence was last modified in	Release 01, July 1986
Annotations were last modified in	Release 40, October 2001

Name and origin of the protein

Protein name	**Chelonianin**
Synonyms	**Basic protease inhibitor** **RTPI**
Gene name	None
From	Caretta caretta (Loggerhead) [TaxID: 8467]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Testudines; Cryptodira; Chelonioidea; Cheloniidae; Caretta.

References

[1] SEQUENCE.
TISSUE=Egg white;
Kato I., Tominaga N.;
"Trypsin-subtilisin inhibitor from red sea turtle eggwhite consists of two tandem domains -- one Kunitz -- one of a new family.";
Fed. Proc. 38:832-832(1979).

Comments

- ***FUNCTION***: THE FIRST DOMAIN INHIBITS TRYPSIN; THE SECOND ONE INHIBITIS SUBTILISIN.
- ***SIMILARITY***: CONTAINS 1 BPTI/KUNITZ INHIBITOR DOMAIN.
- ***SIMILARITY***: CONTAINS 1 WAP-TYPE DOMAIN.
- *CAUTION*: AS THE PAPER ONLY INDICATES THE SPECIES AS "RED SEA TURTLE", THE SPECIES INDICATED HERE IS THEREFORE AN INFERENCE.

Cross-references

EXHIBIT A

PIR	A01224; TITTOR.
HSSP	P00974; 6PTI. [HSSP ENTRY / PDB]
InterPro	IPR002223; Kunitz_BPTI. IPR002221; WAP. Graphical view of domain structure.
Pfam	PF00014; Kunitz_BPTI; 1. PF00095; wap; 1.
PRINTS	PR00003; 4DISULPHCORE. PR00759; BASICPTASE.
ProDom	PD000222; Kunitz_BPTI; 1. [Domain structure / List of seq. sharing at least 1 domain].
SMART	SM00131; KU; 1. SM00217; WAP; 1.
PROSITE	PS00317; 4_DISULFIDE_CORE; 1. PS00280; BPTI_KUNITZ_1; 1. PS50279; BPTI_KUNITZ_2; 1.
BLOCKS	P00993.
ProtoMap	P00993.
PRESAGE	P00993.
DIP	P00993.
ModBase	P00993.
SWISS-2DPAGE	GET REGION ON 2D PAGE.

Keywords

Serine protease inhibitor.

Features

Key	From	To	Length	Description
DOMAIN	8	58	51	BPTI/KUNITZ INHIBITOR.
DOMAIN	63	105	43	WAP.
MOD_RES	1	1		PYRROLIDONE CARBOXYLIC ACID.
DISULFID	8	58		*BY SIMILARITY.*
DISULFID	17	41		*BY SIMILARITY.*
DISULFID	33	54		*BY SIMILARITY.*
DISULFID	67	92		*BY SIMILARITY.*
DISULFID	76	97		*BY SIMILARITY.*
DISULFID	80	93		*BY SIMILARITY.*
DISULFID	86	101		*BY SIMILARITY.*
ACT_SITE	18	19		REACTIVE BOND (TRYPSIN).

Feature aligner

Feature table viewer

Sequence information

Length: **110 AA**	Molecular weight: **11916 Da**	CRC64: **269436243813418E** [This is a checksum on the sequence]

```
        10         20         30         40         50         60
 |      |          |  |       |          |          |          |
QGDKRDICRL PPEQGPCKGR IPRYFYNPAS RMCESFIYGG CKGNKNNFKT KAECVRACRP

        70         80         90        100        110
         |          |          |          |          |
PERPGVCPKT SGPGICLHGC DSDSDCKEGQ KCCFDGCGYI CLTVAPSGSP
```

P00993 in FASTA format

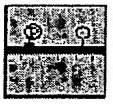
View entry in original SWISS-PROT format
View entry in raw text format (no links)
Report form for errors/updates in this SWISS-PROT entry

Direct BLAST submission at EMBnet-CH/SIB (Switzerland)

Direct BLAST submission at NCBI (Bethesda, USA)

ScanProsite, MotifScan

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)



Feature table viewer (Java)

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